

CLAIMS

- 1) A purified or isolated nucleic acid encoding a mammalian secreted soluble cerebral cortical voltage-dependent calcium channel $\alpha_2\delta$ -2, $\alpha_2\delta$ -3 or $\alpha_2\delta$ -4 subunit polypeptide.
- 2) A purified or isolated nucleic acid according to claim 1, comprising a polynucleotide having at least 90% identity with the sequence encoding :
 - from amino-acid 1 to between amino-acids 1027 and 1062 of SEQ ID N°20 for $\alpha_2\delta$ -2,
 - from amino-acid 1 to between amino-acids 984 and 1019 of SEQ ID N°22 for $\alpha_2\delta$ -3.
- 3) A purified or isolated nucleic acid according to claim 1, having at least 90% identity with the sequence encoding :
 - from amino-acid 1 to between amino-acids 1047 and 1062 of SEQ ID N°20 for $\alpha_2\delta$ -2,
 - from amino-acid 1 to between amino-acids 1004 and 1019 of SEQ ID N°22 for $\alpha_2\delta$ -3.
- 4) A purified or isolated nucleotide sequence according to claim 1 wherein said sequence is the sequence of SEQ ID N°1, SEQ ID N°2, SEQ ID N°3, SEQ ID N°7, SEQ ID N°8, SEQ ID N°9, SEQ ID N°13, SEQ ID N°14, SEQ ID N°15, SEQ ID N°19 or SEQ ID N°21.
- 5) A purified or isolated nucleic acid, having at least 90% identity with the nucleotide sequence of SEQ ID N°19 or SEQ ID N°21.
- 6) A purified or isolated polynucleotide comprising at least 10 consecutive nucleotides of the nucleotide sequence of SEQ ID N°19 or SEQ ID N°21.
- 7) A polynucleotide probe or primer hybridizing, under stringent conditions, with the with the nucleotide sequence of SEQ ID N°19 or SEQ ID N°21.
- 8) A method for the amplification of a nucleic acid encoding a mammalian secreted soluble cerebral cortical voltage-dependent calcium channel $\alpha_2\delta$ -n subunit polypeptide wherein n is 2, 3 or 4, said method comprising the steps of:

- (a) contacting a test sample suspected of containing the target secreted soluble $\alpha_2\delta$ -n subunit nucleic acid, or a sequence complementary thereto, with an amplification reaction reagent comprising a pair of amplification primers located on either side of the $\alpha_2\delta$ -n subunit nucleic acid region to be amplified, and
- 5 (b) optionally, detecting the amplification products.

9) A kit for the amplification of a nucleic acid encoding a secreted soluble $\alpha_2\delta$ -n subunit polypeptide wherein n is 2, 3 or 4, or a complementary sequence thereto in a test sample, wherein said kit comprises:

- 10 (a) a pair of oligonucleotide primers which can hybridize, under stringent conditions, to the secreted soluble $\alpha_2\delta$ -n subunit nucleic acid region to be amplified;
- (b) optionally, the reagents necessary for performing the amplification reaction.

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- 10) A recombinant vector comprising a nucleic acid according to claim 1.
- 11) A recombinant host cell comprising a nucleic acid according to claim 1.
- 12) A method for producing a secreted soluble $\alpha_2\delta$ -n subunit wherein n is 2, 3 or 4, and
- 20 said method comprises the steps of:
- (a) inserting the nucleic acid encoding the desired $\alpha_2\delta$ -n subunit polypeptide in an appropriate vector;
- (b) culturing, in an appropriate culture medium, a host cell previously transformed or transfected with the recombinant vector of step (a);
- 25 (c) harvesting the culture medium thus obtained or lyse the host cell, for example by sonication or osmotic shock;
- (d) separating or purifying, from said culture medium, or from the pellet of the resultant host cell lysate, the thus produced $\alpha_2\delta$ -n subunit polypeptide of interest.

30 13) A purified or isolated recombinant polypeptide comprising the amino acid sequence of a secreted soluble $\alpha_2\delta$ -2, $\alpha_2\delta$ -3 or $\alpha_2\delta$ -4 subunit polypeptide.

14) A recombinant polypeptide according to claim 14, having at least 80% amino-acid identity with a polypeptide comprising:

- from amino acid 1 to between amino acids 1027 and 1062 of the amino acid sequence of SEQ ID N°20, or
- from amino acid 1 to between amino acids 1019 and 1079 of the amino acid sequence of SEQ ID N°22.

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15) A recombinant polypeptide according to claim '14, wherein said recombinant polypeptide is selected from the group consisting of the amino acid sequences of SEQ ID n°4, SEQ ID n°5, SEQ ID n°6, SEQ ID n°10, SEQ ID n°11, SEQ ID n°12, SEQ ID n°16, SEQ ID n°17 and SEQ ID n°18.

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16) A method for the screening of ligands which bind a cerebral cortical voltage-dependent calcium channel $\alpha_2\delta$ -n subunit wherein n is 2, 3 or 4, said method comprising the steps of:

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- contacting a secreted soluble recombinant calcium channel $\alpha_2\delta$ -n subunit polypeptide with:
 - a ligand of interest; and
 - a labelled compound which binds the $\alpha_2\delta$ -n subunit; and
- measuring the level of binding of the labelled compound to the $\alpha_2\delta$ -n subunit.

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17) A method according to claim 16, wherein said method is a scintillation proximity assay.

18) A method according to claim 16, wherein said method is a flashplate assay.

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19) A method according to claim 16, wherein said method is a filter binding assay.

20) A method according to claim 16, wherein said secreted soluble recombinant calcium channel $\alpha_2\delta$ -n subunit polypeptide is selected from polypeptides having at least 80%, preferably 90%, more preferably 95%, and most preferably 98 or 99% amino-acid identity with the polypeptide comprising from amino acid 1 to between amino-acids 984 and 1063, preferably between amino-acids 994 and 1054, and most preferably between amino-acids 1019 and 1054 of SEQ ID N°5 or SEQ ID N°16.

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21) A method according to claim 16, wherein said secreted soluble recombinant calcium channel $\alpha_2\delta$ -n subunit polypeptide is selected from the group consisting of SEQ ID N°6, 7, 8, 9, 13, 14 and 15, with the polypeptides of SEQ ID N°9 and SEQ ID N°15 being most preferred.

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22) A kit for the screening of ligands which bind bind a cerebral cortical voltage-dependent calcium channel $\alpha_2\delta$ -n subunit wherein n is 2, 3 or 4, said kit comprising:

- a secreted soluble recombinant calcium channel $\alpha_2\delta$ -n subunit; and
- a labelled compound which binds to the $\alpha_2\delta$ -n subunit.

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